PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 060210wo HPJ/ko	**FOR FURTHER ACTION**	See Form PCT/IPEA/416
International application No. PCT/EP2005/002975	International filing date *(day/month/year)* 21.03.2005	Priority date *(day/month/year)* 22.03.2004
International Patent Classification (IPC) or national classification and IPC C12Q1/44, C12Q1/04, C12Q1/18		
Applicant GOLDSCHMIDT GMBH et al.		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 13 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☒ *sent to the applicant and to the International Bureau)* a total of 5 sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☒ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the opinion
☒	Box No. II	Priority
☒	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☒	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☒	Box No. VII	Certain defects in the international application
☒	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
20.01.2006	28.03.2006
Name and mailing address of the international preliminary examining authority: European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Authorized Officer Jenkins, G Telephone No. +31 70 340-2608

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/EP2005/002975

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
   - ☐ international search (under Rules 12.3 and 23.1(b))
   - ☐ publication of the international application (under Rule 12.4)
   - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

   Description, Pages

   1-43 as originally filed

   Claims, Numbers

   1-30 received on 20.01.2006 with letter of 20.01.2006

   ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

4. ☒ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
   - ☐ the description, pages
   - ☒ the claims, Nos. 1-30
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/EP2005/002975

Box No. II Priority

1. ☐ This report has been established as if no priority had been claimed due to the failure to furnish within the prescribed time limit the requested:
   ☐ copy of the earlier application whose priority has been claimed (Rule 66.7(a)).
   ☐ translation of the earlier application whose priority has been claimed (Rule 66.7(b)).

2. ☒ This report has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rule 64.1). Thus for the purposes of this report, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application,

   ☒ claims Nos. 1-25,29,30 [w.r.t industrial applicability]

   because:

   ☒ the said international application, or the said claims Nos. 1-25,29,30 [w.r.t industrial applicability] relate to the following subject matter which does not require an international preliminary examination (specify):

   see separate sheet

   ☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

   ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

   ☐ no international search report has been established for the said claims Nos.

   ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	☐	has not been furnished
	☐	does not comply with the standard
the computer readable form	☐	has not been furnished
	☐	does not comply with the standard

   ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

   ☐ See separate sheet for further details

Box No. IV Lack of unity of invention

1. ☐ In response to the invitation to restrict or pay additional fees, the applicant has:
   - ☐ restricted the claims.
   - ☐ paid additional fees.
   - ☐ paid additional fees under protest.
   - ☐ neither restricted nor paid additional fees.

2. ☒ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

   ☐ complied with.

   ☒ not complied with for the following reasons:

   see separate sheet

4. Consequently, this report has been established in respect of the following parts of the international application:

   ☒ all parts.

   ☐ the parts relating to claims Nos. .

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	20
	No:	Claims	1-9,11-19,21-30
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-9,11-30
Industrial applicability (IA)	Yes:	Claims	26-28
	No:	Claims	

2. Citations and explanations (Rule 70.7):

   see separate sheet

Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Re Item I

Basis of the report

1 The claims have been amended throughout by replacing the term "group of organisms" with "population of organisms". There appears to be no literal basis for the term "population of organisms". Furthermore, the skilled person would not necessarily regard the terms "group of organisms" and "population of organisms" to be equivalent. A "population" is a "group", but a "group" is not a "population". In any case, if these terms were to be considered equivalent, then the amendment is unnecessary and cannot serve to establish a contribution over the prior art.

2 Amended claim 1 is now a method for "detecting an effect???" instead of a method for "detecting an enzymatic activity". The claims thus cover any possible "effect???". While the application discloses that microorganisms cause effects (e.g. odour, dandruff etc on p. 2, para. 3), the application in no way discloses that the subject-matter for which protection is sought is directed towards a method of detecting body odour or dandruff, let alone any effect such as scepticemia or AIDS. While it may or may not be obvious to use the methods of the invention to detect body odour or dandruff, it is not directly and unambiguously disclosed in the application as filed. Moreover, the feature "detecting an enzymatic activity" in original claim 1 is an essential feature, and thus cannot be removed without adding subject-matter to the application. In any case, the said "effect???" could be enzymatic activity; therefore this amendment cannot possibly contribute anything towards establishment of novelty or inventive step. By analogy, there is no basis for new dependent claim 10.

3 The claims have been amended throughout by replacing "effect of a substance" with "activity of a substance". There appears to be no literal basis for this amendment, neither is it clear that the terms "effect" and "activity" have exactly the same meaning as one another. If they are equivalent, there should be no need to change the claims.

4 In summary, all the above amendments add subject-matter to the application as filed. They were therefore not taken into account in the below analysis, and no opinion is given for dependent claim 10. The only amendments deemed allowable were the additional features "directly" and "wherein said method is performed in the absence of any culturing step" in amended claim 1.

Re Item II

Priority

5 The priority right of the present application appears invalid for many claims, as the priority document is demonstrably different from the present application.

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

6 Independent claim 1 and all claims dependent thereon involve the step "collecting a sample". While this is admittedly not a method of diagnosis practised on the human or animal body, this step encompasses methods of treatment by surgery such as biopsies, injections etc.

Furthermore, the scope of dependent claims 18-20,22-25,30 relates to a screening method, wherein compounds are contacted with (i.e. administered to) the human or animal body. This both encompasses a method of treatment of the animal or human body by surgery (administering the compounds) and by therapy (the production of therapeutic effects).

Therefore, no opinion is given for the industrial applicability of claims 1-25,29,30 (Rule 67.1(v)). In particular it is not clear from the wording of the claims as whole that the methods are restricted solely to *in vitro* methods carried out on samples collected (i.e. past tense) from an animal or human body.

Re Item IV

Lack of unity of invention

7 DOCUMENTS

D1: LANGLET S ET AL: "A new gel tube method for the direct detection, identification and susceptibility testing of bacteria in clinical samples" FEMS MICROBIOLOGY LETTERS, vol. 170, no. 1, 1 January 1999 (1999-01-01), pages 229-235, XP002343236 ISSN: 0378-1097

D2: US-A-5 098 830 (BAR-OR ET AL) 24 March 1992 (1992-03-24)

D3: US-A-4 603 108 (BASCOMB ET AL) 29 July 1986 (1986-07-29)

D4: DE 196 08 320 A1 (BIOSQUANT GMBH, 15344 STRAUSBERG, DE) 28 August 1997 (1997-08-28)

D5: US 2004/048326 A1 (ROGER-DALBERT CELINE) 11 March 2004 (2004-03-11)

D6: US 2002/031795 A1 (JAMES ARTHUR ET AL) 14 March 2002 (2002-03-14)

D7: WEI G X ET AL: "Proteolysis and utilization of albumin by enrichment cultures of subgingival microbiota" ORAL MICROBIOLOGY AND IMMUNOLOGY, vol. 14, no. 6, December 1999 (1999-12), pages 348-351, XP002343237 ISSN: 0902-0055

D8: LAGARDE D ET AL: "High-throughput screening of thermostable esterases for industrial bioconversions" ORGANIC PROCESS RESEARCH AND DEVELOPMENT, CAMBRIDGE, GB, vol. 6, no. 4, 27 June 2002 (2002-06-27), pages 441-445, XP002288681

D9: DATABASE WPI Section Ch, Week 200308 Derwent Publications Ltd., London, GB; Class B05, AN 2003-084866 XP002288684 & JP 2002 326942 A (NONOGAWA SHOJI KK) 15 November 2002 (2002-11-15)

D10: US 2003/199017 A1 (REYMOND JEAN-LOUIS ET AL) 23 October 2003 (2003-10-23)

D11: JAEGER K-E ET AL: "BACTERIAL LIPASES" FEMS MICROBIOLOGY REVIEWS, ELSEVIER, AMSTERDAM, NL, vol. 15, no. 1, January 1994 (1994-01), pages 29-63, XP000490500 ISSN: 0168-6445

8 According to the description (p. 1, paragraph 1), the problem to be solved in the present application relates to detection of organisms in a sample without previously culturing the microorganisms. The technical solution as laid out in the present claims is to use substrates transformable by an enzymatic activity. The single general concept which can be identified as *a priori* linking the various claimed inventions is the notion that substrates transformable by an enzymatic activity can be used for detection of organisms in a sample without previously culturing the microorganisms

9 D1 discloses: a method for the direct (i.e. without any culturing: p. 229, column 2) detection of *E. coli* in urine samples involving contacting the sample with methylumbelliferyl substrate and detecting transformation of the substrate by *E. coli* beta-glucuronidase (p. 231; fig, 1)

10 D2 discloses: a method for direct detection of *C. albicans* on a vaginal swab that has not been subjected to a culturing step (claim 1, last line) involving contacting the sample with methylumbelliferyl substrate and detecting transformation of the substrate by *C. albicans* peroxidase (claim 1; c. 3-5).

11 D3 discloses a method for detection and identification of microorganisms directly on clinical samples using a range of detectable substrates specifically transformable by a range of particular microorganisms (c. 3, l. 4-20; c. 4, l. 64-70).

12 D4 discloses a method for detection and identification of microorganisms directly in water samples using detectable substrates specifically transformable by microorganisms found in unsafe drinking water (c. 2, l. 67 - c. 3, l. 3).

13 In light of these documents, the above identified single general concept is not new and can thus not be the single general inventive concept as required by Rule 13.1 PCT. The present application is therefore considered not to fulfil the requirement of unity as laid down in Rule 13.1 PCT. The objective problem is therefore to provide further substrates transformable by an enzymatic activity that can be used for detection of organisms in a sample without previously culturing the microorganisms. Each of the different substrates of the present application is then a separate solution to this problem not sharing a special technical feature in the sense of Rule 13.2 PCT.

14 Consequently, the groups of inventions are split up as follows: 1) 2-hydroxy-4-p-nitrophenoxy-butyl decanoate / hexanoate for detecting lipase activity in skin and *Bacillus* microorganisms without previously culturing the microorganisms (claims 10-13,27 [full], 1-9,14-26,28,29 [partial]); 2) casein-resorufin for detecting protease activity in *Bacillus* microorganisms without previously culturing the microorganisms (claims 14 [full], 1-9,14-26,28,29 [partial]). No other technical features could be identified that form a technical relationship among each of the separate inventions claimed and which could be considered as a special technical feature within the meaning of Rule 13.2 PCT.

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability;

citations and explanations supporting such statement.

15 NOVELTY

16 The subject-matter of claims 1-18,20-29 is not new (Article 33(2) PCT).

17 D1 discloses: a method for direct (i.e. without any culturing: p. 229, column 2) detection of *E. coli* in urine samples involving contacting the sample with methylumbelliferyl substrate and detecting transformation of the substrate by E. coli beta-glucuronidase (p. 231; fig, 1). A kit containing a sampling tool (note: this could be any common laboratory implement such as spatulas, tweezers, measuring devices) and a transformable substrate is therefore implicitly disclosed. The subject-matter of claims 1-3,5-8,16,17,26,27,29 is therefore not new (Article 33(2) PCT).

18 D2 discloses: a method for direct detection of *C. albicans* on a vaginal swab that has not been subjected to a culturing step (claim 1, last line) involving contacting the sample with methylumbelliferyl substrate and detecting transformation of the substrate by *C. albicans* peroxidase (claim 1; c. 3-5). The subject-matter of claims 1-9,16,17,26,27,29 is therefore not new (Article 33(2) PCT).

19 D3 discloses a method for detection and identification of microorganisms directly on clinical samples using a range of detectable substrates specifically transformable by a range of particular microorganisms (c. 3, l. 4-20; c. 4, l. 64-70). The subject-matter of claims 1-9,16,17,26,27,29 is therefore not new (Article 33(2) PCT).

20 D4 discloses a method for detection and identification of microorganisms directly in water samples using detectable substrates specifically transformable by microorganisms found in unsafe drinking water (c. 2, l. 67 - c. 3, l. 3). The subject-matter of claims 1-3,5-9,16,17,26,27,29 is therefore not new (Article 33(2) PCT).

21 D5 discloses a method for detection of *Salmonella* strains involving direct inoculation of collected samples into a culture medium containing chromogenic or fluorogenic esterase substrates (paragraphs [0021], [0028]; examples 1 and 2). The subject-matter of claims 26,27 is therefore not new (Article 33(2) PCT).

22 D6 discloses a method for detection of bacteria involving direct addition of a sample

and nitrocoumarin detectable substrate to a culture medium (paragraphs 27-29). The subject-matter of claims 26,27 is therefore not new (Article 33(2) PCT).

23 D7 discloses a method for detection of microorganisms of sub-gingival plaque by detection of the transformation of resorufin-labelled casein by microbial proteases. Here, the sample is collected from a culture (p. 349, c. 2, last paragraph). D7 is prejudicial to the novelty of claims 26,27 (Article 33(2) PCT).

24 D8 discloses a method for detecting microorganisms that have a thermostable esterase involving collecting a sample from a cell culture, contacting with 2-hydroxy-4-p-nitrophenoxy-butyl decanoate, and measuring conversion thereof (p. 442, column 2). The subject-matter of claims 26-28 is therefore not new (Article 33(2) PCT).

25 D9 (WPI abstract) discloses a method of identifying compounds useful in the treatment of acne and rough skin involving testing the ability of a candidate compound to inhibit microbial lipase activity, which is detected by transformation of 4-methyl umbelliferyl oleate. Note, there is no culture step between collecting a sample of microbes and contacting with the transformable substrate. The subject-matter of claims 26,27 is therefore not new (Article 33(2) PCT).

26 By the applicant's own admissions (application, p. 16, l. 10-20), D10 discloses derivatives of 4-umbelliferyloxy-1,2-butanediol and 4-nitrophenyloxy-1,2-butanediol. D10 also implicitly discloses objects that could serve as sampling tools. The subject-matter of claims 26-27 is therefore not new (Article 33(2) PCT).

27 INVENTIVE STEP

28 The subject-matter of claim 20 merely adds routine modification options to the subject-matter of claim 1 and is therefore obvious to a person skilled in the art. For this reason the subject-matter of said claims does not involve an inventive step in the sense of Article 33(3) PCT.

29 INDUSTRIAL APPLICABILITY

30 The subject-matter of claims 26-28 is considered industrially applicable (Article 33(4) PCT).

Re Item VII

Certain defects in the international application

31 The independent claims of the present application are not in the two-part form in accordance with Rule 6.3(b) PCT. It is felt that it would be essential to use such a form in any set of amended claims as it is so unclear what the applicant considers the special technical features of the present application to be.

Re Item VIII

Certain observations on the international application

32 The present claims are *in extremis* broad in relation to the contribution to the art and several essential features appear to be missing from independent claim 1, contrary to Article 6 PCT. Furthermore, there are too many claims in relation to nature of the alleged invention, contrary to the requirements of conciseness of Article 6 PCT. The lack of conciseness makes it unduly burdensome for the skilled person to determine the intended scope of protection.

33 Firstly, it is noted that the technical aim as laid out in the description is to provide a method that does not require time-consuming culturing steps (p. 10; p. 13, l. 5-10). However, the characterising part of independent claim 1 has been defined solely in terms of the technical problem ("wherein said method is performed in the absence of any culture step"), rather than in terms of the technical elements required to solve the problem. Thus, claim 1 is a result to be achieved, contrary to Article 6 PCT). The skilled person needs to know what technical elements are required to achieve this effect (i.e. the specific substrates, enzymes, and target microorganisms).

34 More fundamentally, there is grave lack of support and disclosure for the subject-matter of independent claim 1 across the whole of the claimed scope. The claims cover detecting any organism (i.e. including non-cultivable organisms) by detecting any enzyme activity with any substrate. Indeed the method is not even limited to microorganisms. However, the examples only show three specific substrates that can be used to detect specific enzyme activities in specific microorganisms without any cultivation step (2-hydroxy-4-p-nitrophenoxy-butyl decanoate / hexanoate for lipase activity and casein-resorufin for protease activity in Bacillus microorganisms). The

person skilled in the art would not know from common general knowledge in combination with the present disclosure what other substrates could be used to detect other particular types of enzyme found in other particular groups of organisms without involving a culturing step. Indeed, by the applicant's own admissions (e.g. p. 3), it is customary in the art to always incorporate cultivating / culturing into methods for detecting microorganisms so the skilled person would not expect the present method to work for any substrate / enzyme / microorganism combination. Finally, for 4-umbelliferyloxy-1,2-butanediols (claim 10), no such technical teaching has been established in the application as filed. As such, the subject-matter of the present claims is considered to be unsupported (Article 6 PCT) and undisclosed in the application as a whole (Article 5 PCT), since the claims are not restricted to 2-hydroxy-4-p-nitrophenoxy-butyl decanoate / hexanoate for lipase activity and casein-resorufin for protease activity in Bacillus strains.

CONCLUSION: Overall, significant amendments would be required to bring the present application into compliance with the requirements of the PCT. The seemingly trivial amendments made during the international preliminary examination appear in no way to represent a *bona fide* effort to overcome the fundamental and well-founded objections raised, rather they create more problems than they solve.

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Claims:

1. A method to detect directly an effect caused by a population of organisms, comprising the steps of:

   a) determining an enzymatic activity specifically shared by the population of organisms responsible of said effect
   b) selecting a substrate transformable by the shared enzymatic activity determined at step a),
   c) collecting a sample suspected to contain said population of organisms,
   d) contacting said collected sample with the substrate selected at step b),
   e) detecting and optionally quantifying the amount of transformed substrate,

wherein said method is performed in the absence of any culture step.

2. The method according to claim 1, wherein the sample is collected on a surface or in a liquid.

3. The method according to claim 2, wherein the surface is any part of an object, of food, of a plant, of an animal or human body.

4. The method according to the previous claim 3, wherein the part of an animal or human body is skin, hair, nails, eyes, teeth, or mucous membranes.

5. The method according to the claim 2, wherein the liquid is from an environment, from food, from plants, from industrial wastes, from an animal or human body.

6. The method according to claim 1 wherein the population of organisms is a population of microorganisms.

7. The method according to claim 6 wherein the population of microorganisms consists of bacteria, fungi, yeasts, viruses, protists, archaebacteria, or eukaryotes.

8. The method according to claim 1, wherein the enzymatic activity is either an oxidoreductase, a transferase, an hydrolase, a lyase, an isomerase, a ligase, or any combination thereof.

9. The method according to claim 1, wherein the enzymatic activity is the activity of a reductase, an alcohol dehydrogenase, an alcohol oxidase, an amino acid oxidase, a monooxygenase, a dioxygenase, an amidase, an acylase, a lyase, a xylanase, a protease, a nitrilase, a nitrile hydratase, an epoxide hydrolase, a lipase or an esterase.

10. The method according to claim 1, wherein the enzymatic activity is the activity of lipase and esterase and the effect is an odor

11. The method according to claim 8, wherein the selected substrate is a derivative of 4-nitrophenyloxy-1,2-butanediol or 4-umbelliferyloxy-1,2-butanediol and can be transformed by the enzymatic activity.

12. The method according to claim 8, wherein the transformable substrate is an ester when the population of organism shares an esterase activity.

13. The method according to claim 9, wherein the ester is a 2-hydroxy-4-p-nitrophenoxy-butyl carboxylic acid ester.

14. The method according to claim 11, wherein the 2-hydroxy-4-p-nitrophenoxy-butyl carboxylic acid ester is the 2-hydroxy-4-p-nitrophenoxy-butyl hexanoate or the 2-hydroxy-4-p-nitrophenoxy-butyl decanoate.

15. The method according to claim 8, wherein the transformable substrate is the casein resorufin when the population of organism shares a protease activity.

16. The method according to claim 1, wherein the transformed substrate is directly detectable, or it is detectable after at least one additional step following the enzymatic step.

17. The method according to claim 1, wherein the amount of transformed substrate is compared with an amount of transformed substrate obtained in at least one control.

18. A method for the evaluation of the activity of a substance of interest expected to act on a population of organisms, , wherein the method according to claim 1 is performed before and after contacting said substance with the surface or liquid containing the population of organisms, and wherein the variation of the transformed substrate is measured between both situations.

19. A method for the evaluation of the activity of a substance of interest expected to act on a population of organisms, , wherein the method according to claim 1 is performed in the presence and in the absence of said

substance and wherein the variation of the transformed substrate is measured between both situations.

20. A method for the evaluation of the activity of a substance according to claims 18 and 19 wherein said substance and said sample are put together before the collecting of said sample.

21. A method for the evaluation of the activity of a substance according to claims 18 and 19 wherein said substance and sample are put together after the collecting of said sample.

22. A screening method of different substances of interest expected to act on a population of organisms, wherein the method according to claim 1 is performed with said substances and wherein the best substance is selected on the basis of the amount of transformed substrate in the presence of said best substance as compared to the other ones.

23. The method according to claims 18 to 21, wherein the substance of interest is a chemical, biological, pharmaceutical, cosmetic, veterinary or agricultural substance.

24. The method according to claim 23, wherein the substance of interest is an antimicrobial substance.

25. The method according to claim 24, wherein the substance of interest is an anti-acne composition, a deodorant or a shampoo, preferably an anti-dandruff shampoo.

26. A kit for the detection of an effect caused by a population of organisms, according to the method of claim 1, said kit comprising

a) a sampling tool,

b) a substrate transformable by an enzymatic activity shared by said population of organisms,
c) if required reagents for the detection of the transformable substrate,
d) optionally controls.

27. A kit for the evaluation of the activity of a substance of interest expected to act on a population of organisms, cultivable or not cultivable, said kit comprising
a) a sampling tool,
b) a substrate transformable by an enzymatic activity shared by said population of organisms,
c) optionally a sample control,
d) if required reagents for the detection of the transformable substrate.

28. A kit for the evaluation of the activity of a deodorant, according to claim 26, said kit comprising
a) sample tool,
a) 2-hydroxy-4-p-nitrophenoxy-butyl decanoate,
b) a control,
c) reagents for the detection of the 2-hydroxy-4-p-nitrophenoxy-butyl decanoate.

29. The use of a method according to any of claims 1 to 17 in order to achieve the detection and/or quantification of a population of organisms,.

30. The use of a method according to any of claims 1 to 25 in order to achieve the evaluation of the activity of a substance of interest.